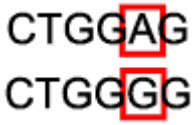
Types of mutations

There are many different ways that DNA can be changed, resulting in different types of mutation. Here is a quick summary of a few of these:

Substitution

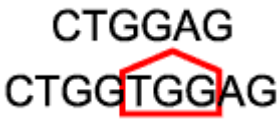
A substitution is a mutation that exchanges one base for another (i.e., a change in a single "chemical letter" such as switching an A to a G). Such a substitution could:

1. change a codon to one that encodes a different amino acid and cause a small change in the protein produced. For example, sickle cell anemia is caused by a substitution in the beta-hemoglobin gene, which alters a single amino acid in the protein produced.
2. change a codon to one that encodes the same amino acid and causes no change in the protein produced. These are called silent mutations.
3. change an amino-acid-coding codon to a single "stop" codon and cause an incomplete protein. This can have serious effects since the incomplete protein probably won't function.



Insertion

Insertions are mutations in which extra base pairs are inserted into a new place in the DNA.

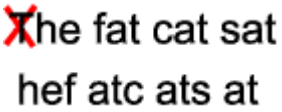


Deletion

Deletions are mutations in which a section of DNA is lost, or deleted.

Frameshift

Since protein-coding DNA is divided into codons three bases long, insertions and deletions can alter a gene so that its message is no longer correctly parsed. These changes are called frameshifts.
For example, consider the sentence, "The fat cat sat." Each word represents a codon. If we delete the first letter and parse the sentence in the same way, it doesn't make sense.
In frameshifts, a similar error occurs at the DNA level, causing the codons to be parsed incorrectly. This usually generates truncated proteins that are as useless as "hef atc ats at" is uninformative.
There are other types of mutations as well, but this short list should give you an idea of the possibilities.

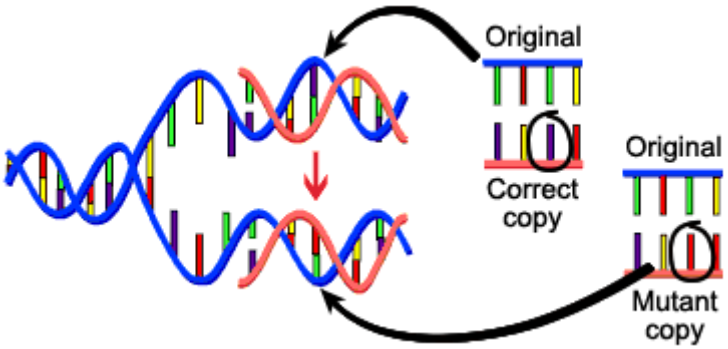


The causes of mutations

Mutations happen for several reasons.

1. DNA fails to copy accurately

Most of the mutations that we think matter to evolution are "naturally-occurring." For example, when a cell divides, it makes a copy of its DNA — and sometimes the copy is not quite perfect. That small difference from the original DNA sequence is a mutation.



2. External influences can create mutations

Mutations can also be caused by exposure to specific chemicals or radiation. These agents cause the DNA to break down. This is not necessarily unnatural — even in the most isolated and pristine environments, DNA breaks down. Nevertheless, when the cell repairs the DNA, it might not do a perfect job of the repair. So the cell would end up with DNA slightly different than the original DNA and hence, a mutation.

The effects of mutations

Since all cells in our body contain DNA, there are lots of places for mutations to occur; however, some mutations cannot be passed on to offspring and do not matter for evolution. Somatic mutations occur in non-reproductive cells and won't be passed onto offspring. For example, the golden colour on half of this Red Delicious apple was caused by a somatic mutation. Its seeds will not carry the mutation.

The only mutations that matter to large-scale evolution are those that can be passed on to offspring. These occur in reproductive cells like eggs and sperm and are called germ line mutations.

Effects of germ line mutations

A single germ line mutation can have a range of effects:

1. **No change occurs in phenotype.**
   Some mutations don't have any noticeable effect on the phenotype of an organism. This can happen in many situations: perhaps the mutation occurs in a stretch of DNA with no function, or perhaps the mutation occurs in a protein-coding region, but ends up not affecting the amino acid sequence of the protein.

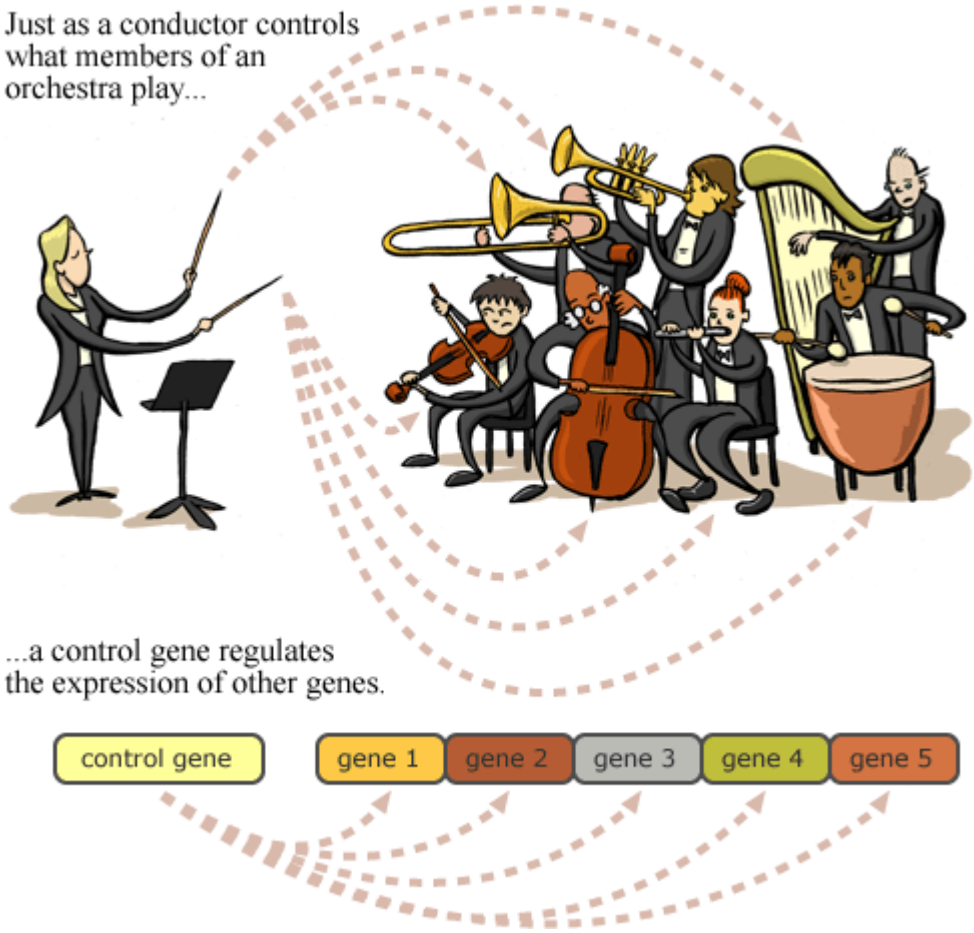
2. **Small change occurs in phenotype.**
   A single mutation caused this cat's ears to curl backwards slightly.

3. **Big change occurs in phenotype.**
   Some really important phenotypic changes, like DDT resistance in insects are sometimes caused by single mutations. A single mutation can also have strong negative effects for the organism. Mutations that cause the death of an organism are called lethals — and it doesn't get more negative than that.

Little mutations with big effects: Mutations to control genes

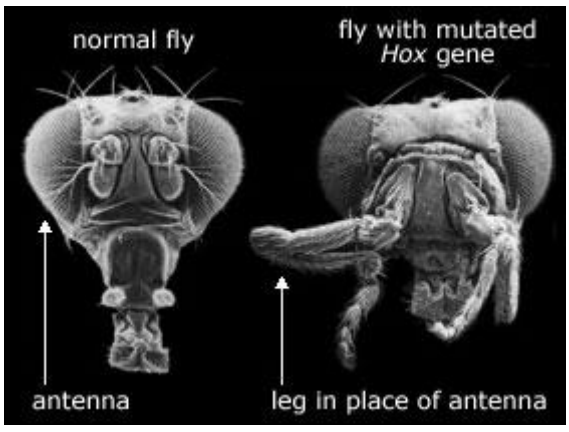
Mutations are often the victims of bad press — unfairly stereotyped as unimportant or as a cause of genetic disease. While many mutations do indeed have small or negative effects, another sort of mutation gets less airtime. Mutations to control genes can have major (and sometimes positive) effects.

Some regions of DNA control other genes, determining when and where other genes are turned "on". Mutations in these parts of the genome can substantially change the way the organism is built. The difference between a mutation to a control gene and a mutation to a less powerful gene is a bit like the difference between whispering an instruction to the trumpet player in an orchestra versus whispering it to the orchestra's conductor. The impact of changing the conductor's behavior is much bigger and more coordinated than changing the behavior of an individual orchestra member. Similarly, a mutation in a gene "conductor" can cause a cascade of effects in the behavior of genes under its control.



Many organisms have powerful control genes that determine how the body is laid out. For example, *Hox* genes are found in many animals (including flies and humans) and designate where the head goes and which regions of the body grow appendages. Such master control genes help direct the building of body "units," such as segments, limbs, and eyes. So evolving a major change in basic body layout may not be so unlikely; it may simply require a change in a Hox gene and the favor of natural selection.

Mutations to control genes can transform one body part into another. Scientists have studied flies carrying *Hox* mutations that sprout legs on their foreheads instead of antennae!

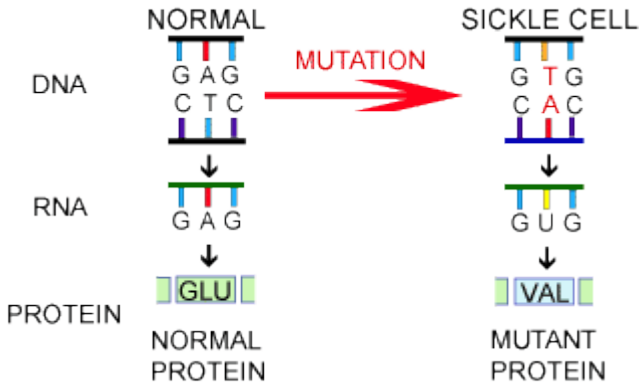


A case study of the effects of mutation: Sickle cell anaemia

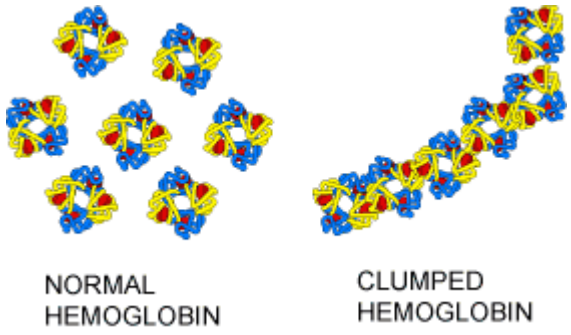
Sickle cell anaemia is a genetic disease with severe symptoms, including pain and anaemia. The disease is caused by a mutated version of the gene that helps make haemoglobin — a protein that carries oxygen in red blood cells. People with two copies of the sickle cell gene have the disease. People who carry only one copy of the sickle cell gene do not have the disease, but may pass the gene on to their children.

The mutations that cause sickle cell anaemia have been extensively studied and demonstrate how the effects of mutations can be traced from the DNA level up to the level of the whole organism. Consider someone carrying only one copy of the gene. She does not have the disease, but the gene that she carries still affects her, her cells, and her proteins:

1. **There are effects at the DNA level**

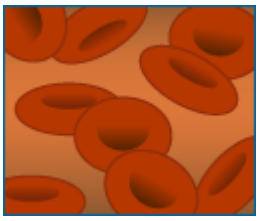


2. **There are effects at the protein level**



Normal haemoglobin (left) and haemoglobin in sickled red blood cells (right) look different; the mutation in the DNA slightly changes the shape of the haemoglobin molecule, allowing it to clump together.

3. **There are effects at the cellular level**
   When red blood cells carrying mutant hemoglobin are deprived of oxygen, they become "sickle-shaped" instead of the usual round shape (see picture). This shape can sometimes interrupt blood flow.



4. **There are negative effects at the whole organism level**
   Under conditions such as high elevation and intense exercise, a carrier of the sickle cell allele may occasionally show symptoms such as pain and fatigue.

5. **There are positive effects at the whole organism level**
   Carriers of the sickle cell allele are resistant to malaria, because the parasites that cause this disease are killed inside sickle-shaped blood cells.

Normal red blood cells (top) and sickle cells (bottom)

This is a chain of causation. What happens at the DNA level propagates up to the level of the complete organism. This example illustrates how a single mutation can have a large effect, in this case, both a positive and a negative one. But in many cases, evolutionary change is based on the accumulation of many mutations, each having a small effect. Whether the mutations are large or small, however, the same chain of causation applies: changes at the DNA level propagate up to the phenotype.